

## CLAIMS

1. A cell-specific expression/replication vector that does not act to adult normal cells, wherein a transcriptional initiation regulatory region of a gene that expresses cell-specifically is integrated upstream of a predetermined gene, and a thymidine kinase gene that exists in said cell-specific expression/replication vector is used to suppress the replication at a desired period.

2. The cell-specific expression/replication vector that does not act to adult normal cells according to claim 1, wherein the transcriptional initiation regulatory region of the gene that expresses cell-specifically is a region including the base sequence shown in Seq. ID No. 1.

3. The cell-specific expression/replication vector that does not act to adult normal cells according to claim 2, wherein the region including the base sequence shown in Seq. ID No. 1 is a region including a human calponin gene promoter comprising a base sequence shown in Seq. ID No. 2.

4. The cell-specific expression/replication vector that does not act to adult normal cells according to claim 3, wherein the region including a base sequence shown in Seq. ID No. 2 is a region including a base sequence shown in Seq. ID No. 3.

5. The cell-specific expression/replication vector that does not act to adult normal cells according to claim 1, wherein the transcriptional initiation regulatory region of the gene that

expresses cell-specifically comprises a base sequence wherein one or a few base is deleted, substituted or added in a base sequence shown in Seq. ID No. 1, Seq. ID No. 2 or Seq. ID No. 3, and is a region including a base sequence having a transcription initiation control activity.

6. The cell-specific expression/replication vector that does not act to adult normal cells according to any one of claims 1 to 5, wherein an enhancer is integrated upstream of the transcriptional initiation regulatory region.

7. The cell-specific expression/replication vector that does not act to adult normal cells according to claim 6, wherein the enhancer is a 4F2 enhancer.

8. The cell-specific expression/replication vector that does not act to adult normal cells according to any one of claims 1 to 7, wherein a DNA that encodes a desired protein different from the predetermined gene is linked further downstream on the predetermined gene, and expresses the desired protein under the control of said transcriptional initiation regulatory region.

9. The cell-specific expression/replication vector that does not act to adult normal cells according to claim 8, wherein the DNA that encodes the desired protein is linked to the predetermined gene via an IRES (internal ribosomal entry site).

10. The cell-specific expression/replication vector that does not act to adult normal cells according to any one of claims 1 to 9, wherein the DNA that encodes the desired protein is an

apoptosis promotion-related gene.

11. The cell-specific expression/replication vector that does not act to adult normal cells according to any one of claims 1 to 9, wherein the DNA that encodes the desired protein is a DNA that encodes a protein having a suppressive action of angiogenesis.

12. The cell-specific expression/replication vector that does not act to adult normal cells according to any one of claims 1 to 9, wherein the DNA that encodes the desired protein is a DNA that encodes a protein having a suppressive action against cancer metastasis.

13. The cell-specific expression/replication vector that does not act to adult normal cells according to any one of claims 1 to 9, wherein the DNA that encodes the desired protein is a DNA that encodes a protein having a suppressive action against cancer growth.

14. The cell-specific expression/replication vector that does not act to adult normal cells according to any one of claims 1 to 13, wherein the predetermined gene is a viral replication-related gene.

15. The cell-specific expression/replication vector that does not act to adult normal cells according to claim 14, wherein the viral replication-related gene is ICP4 or E1A.

16. The cell-specific expression/replication vector that does

not act to adult normal cells according to any one of claims 1 to 15, wherein the expression/replication vector is a viral vector.

17. The cell-specific expression/replication vector that does not act to adult normal cells according to claim 16, wherein the viral vector is a herpes simplex virus vector (HSV vector) or an adenoviral vector.

18. The cell-specific expression/replication vector that does not act to adult normal cells according to any one of claims 1 to 17, wherein the vector is tumor cell-specific, proliferating smooth muscle-specific in tumor neovasculature, proliferating smooth muscle-specific in proliferating vascular lesion, proliferating mesangial cell-specific in glomerulonephritis, or proliferating myofibroblast-specific in fibrosis.

19. The cell-specific expression/replication vector that does not act to adult normal cells according to any one of claims 1 to 18, wherein a DNA that encodes ribonucleotide reductase is deleted.

20. A method for expression/replication of a gene, protein or a peptide of a cell-specific expression/replication vector that does not act to adult normal cells, wherein the cell-specific expression/replication vector that does not act to adult normal cells according to any one of claims 1 to 19 is introduced into the cells and tissues of an organism, then expressed and replicated.

21. A method for suppressing the expression/replication of a gene, protein or a peptide of a cell-specific expression/replication vector that does not act to adult normal cells, wherein the cell-specific expression/replication vector that does not act to adult normal cells according to any one of claims 1 to 19 is introduced into the cells and tissues of an organism, then expressed and replicated, and the expression/replication of the cell-specific expression/replication vector is suppressed at a later desired period.

22. The method for suppressing the expression/replication of a gene, protein or a peptide of a cell-specific expression/replication vector that does not act to adult normal cells according to claim 21, wherein the suppression of the expression/replication of the cell-specific expression/replication vector is a suppression by using antiviral drugs including aciclovir and ganciclovir.

23. A method for detecting the in vivo distribution of a cell-specific expression/replication vector that does not act to adult normal cells, wherein the cell-specific expression/replication vector that does not act to adult normal cells according to any one of claims 1 to 19 is introduced into the cells and tissues of an organism, then expressed and replicated, and the thymidine kinase activity by said cell-specific expression/replication vector is determined.

24. The method for detecting the in vivo distribution of a

cell-specific expression/replication vector that does not act to adult normal cells according to claim 23, wherein the determination of the thymidine kinase activity is a determination by positron emission tomography using an uracil derivative FIAU labeled with  $^{124}\text{I}$ .

25. The method according to any one of claims 20 to 24, wherein the cells and tissues in the organism are tumor tissues, vascular or lymphatic vessel constriction tissues, nephritic tissues or fibrotic tissues.

26. A therapeutic drug comprising the cell-specific expression/replication vector that does not act to adult normal cells according to any one of claims 1 to 19.

27. The therapeutic drug according to claim 26, wherein the therapeutic drug is against malignant tumor, fibrosis, proliferating vascular lesion or proliferating glomerulonephritis.

28. The therapeutic drug according to claim 27, wherein the therapeutic drug is against malignant fibrous histiocytoma, gastrointestinal stromal tumor or uterine myoma.

29. A therapeutic method for fibrosis and malignant tumor, wherein the cell-specific expression/replication vector that does not act to adult normal cells according to any one of claims 1 to 19 is introduced into fibrotic tissues including lung and liver, or malignant tumor tissues including breast cancer, gastric cancer and pancreatic cancer, then a proliferating

myofibroblast is selectively disrupted as a result of replication of a vector, and expression of a gene, protein and a peptide.

30. The therapeutic method for fibrosis and malignant tumor according to claim 29, wherein its subject is leiomyosarcoma, malignant fibrous histiocytoma, gastrointestinal stromal tumor or uterine myoma.

31. A therapeutic method for proliferating vascular lesion, wherein the cell-specific expression/replication vector that does not act to adult normal cells according to any one of claims 1 to 19 is introduced into blood vessel or lymphatic vessel constriction tissues or arteriosclerotic tissues and tissues with diabetic retinopathy, then a proliferating smooth muscle cell or a perivascular cell is selectively disrupted as a result of replication of a vector, and expression of a gene, protein or a peptide.

32. A therapeutic method for proliferating glomerulonephritis, wherein the cell-specific expression/replication vector that does not act to adult normal cells according to any one of claims 1 to 19 is introduced into a nephritic tissue, then a proliferating mesangial cell is selectively disrupted as a result of replication of a vector, and expression of a gene, protein or a peptide.

33. The therapeutic method according to any of claims 29 to 32, wherein the cell-specific expression/replication vector is administered to a vein or artery.

34. The therapeutic method according to any one of claims 29 to 33, wherein the expression/replication of the cell-specific expression/replication vector is suppressed at a desired period.

35. A method for producing a cell-specific expression/replication vector, wherein a virus mixed solution after homologous recombination including the cell-specific expression/replication vector according to any one of claims 1 to 19 is infected to a cell wherein the transcriptional initiation regulatory region of a gene that expresses cell-specifically can be activated or a cell that expresses said gene, and the expression of a gene integrated in the vector is used as an index to purify to a single clone by limiting dilution without using agarose overlay assay.

36. The method for producing the cell-specific expression/replication vector according to claim 35, wherein the cell is an ICP4 non-expressing cell.